# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/665,864 | 09/18/2003 | Zhuyin Julie Li | USA V2002/0121 US NP | 8381 |

5487 7590 02/07/2008

ANDREA Q. RYAN
SANOFI-AVENTIS U.S. LLC
1041 ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

| EXAMINER |
|---|
| KIM, TAEYOON |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 02/07/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatent.E-Filing@sanofi-aventis.com
andrea.ryan@sanofi-aventis.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/665,864 | LI ET AL. | |
| | Examiner | Art Unit | |
| | Taeyoon Kim | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/7/2007 has been entered.

Applicant's amendment and response filed on 5/25/2007 has been received and entered into the case.

Claims 1-25 are pending and have been considered on the merits. All arguments have been fully considered.

In the response to the previous office action, applicant argued that advantages of the instant invention over the prior art, such as unexpected results, need not be claimed. Further applicant indicates that such advantages can be introduced in evidence in a declaration under rule 132. The examiner agrees with the applicant that such unexpected result can be evidenced by filing C.F.R. §1.132 declaration. However, there has been no declaration filed in the current application providing evidence showing that the current invention has unexpected results over the prior art cited in the previous office action. Furthermore, the unexpected results asserted by the applicant are shortening duration of assay time and/or simpler steps available using the instant invention. As discussed in the previous office action, the current invention, especially in

claims 2 and 3, claims that the duration of incubation time being at least about 10 minutes or the duration being ranging from about 10 minutes to at least about 2 hours. These limitations are considered to be open-ended and encompassing any duration of incubation time. Based on such broader limitation disclosed in the claims, the method of prior art clearly within the range of such limitation. Furthermore, a person of ordinary skill in the art would recognize that shortening of assay time is desired in any assay method of interest, and thus it would have been obvious to a person of ordinary skill in the art to try to reduce duration of incubation and any unnecessary steps present in the method of the prior art. The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Furthermore, the duration of incubation time would be considered to be a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter

encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed atl a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Decker et al. (Clin. Caner Res. 1999) in view of Corominas et al. (JBC, 1985) and Armstrong et al. (Anal. Biochem. 2001).

Claims 1-25 are drawn to a method determining the activity of PARP comprising the steps of (i) incubating a mixture of activated PARP enzyme, a compound or an agent, and a substrate reagent solution comprising fluorescence-labeled NAD, DNA and histone, (ii) illuminating the mixture with plane polarized light, and measuring polarization, and comparing the measurement between the compound or agent and a control, and limitations to the fluorescence label, duration of incubation are also disclosed.

It is noted that the amendment filed on 5/25/2007 discloses a new limitation of transitional phrase. The previous "comprising of" has been switched to "consisting essentially of". M.P.E.P. § 2111.03 clearly indicates that the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original). "A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims

that are drafted in a 'comprising' format." *PPG Industries v. Guardian Industries*, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998), *et al.* For the purposes of searching for and applying prior art under 35 U.S.C. §§ 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." **If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention**. *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964) *et al.* Since the specification in this case does not particularly point out the basic and novel characteristics of the claimed composition, "consisting essentially of" in claim 1 has been interpreted as "comprising" for the purpose of art rejections.

Decker discloses a PARP inhibition assay which differs from that recited in the claims in that Decker does not use fluorescently labeled NAD in the quantification of enzyme activity. See, e.g., Fig 1, on page 1170. However, Corominas et al. clearly discloses that labeled NAD can be used in the quantification of PARP activity. See, e.g., page 16270, left column. Moreover, Armstrong discloses the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme, an assay which detects similar activity to that of both Decker and Corominas. See, e.g., page 28. Thus, the artisan of ordinary skill would have considered it obvious to have used fluorescently labeled NAD in the quantification of enzyme activity in Decker's assay, motivation for such practice

being derived from Corominas' disclosure of the suitability of labeled NAD as detection moiety in PARP assays, and from Armstrong's disclosure of the suitability of fluorescently labeled NAD as a detection moiety in a similar assay of ADP-ribosylating enzyme. Moreover, the selection of known fluorescent moieties, and the determination of suitable linking moieties therefor as recited in the claims under examination, would have been considered obvious in view of the cited references' disclosures of the suitability of using fluorescently labels to detect NAD. A holding of obviousness is therefore required.

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trevigen (Universal Colorimetric PARP Assay kit with histones and coating buffer, 2000; http://www.trevigen.com/Protocols/4671_4672-096-K.pdf) in view of Armstrong et al. (supra), Sundberg (Current Opinion in Biotechnology, 2000, 11:47–53) and Human Molecular Genetics (Fluorescence labeling and detection system, 1999; http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.table.479)

It is noted that although the published date of the Trevigen article is not clearly established, this assay kit utilizing a biotinylated NAD+ for PARP assay has been disclosed by an article entitled to New Technology (Nature Medicine, 2000, 6:715; ). Therefore, the Examiner considers the reference as a prior art to the filing date of the current application.

The Trevigen reference teaches a method of determining inhibitors on the activity of PARP comprising steps of incubation of PARP enzyme, an inhibitor, a substrate (biotinylated NAD+, DNA, histone), detection of enzymatic activity, and comparison of

the measurement (see pages 1-4).

The Trevigen article does not teach the use of fluorescently labeled NAD+ in an assay.

Armstrong et al. teach the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme.

Sundberg teaches fluorescence-based biochemical assays.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute biotinylated NAD+ of Trevigen with fluorescently labeled NAD+ of Armstrong et al. in the method of Trevigen Instruction.

The skilled artisan would have been motivated to make such a modification because Sundberg teach that fluorescence-based detection methods are inherently sensitive due to the short duty cycle of most fluorophores (the fluorescence lifetime of fluorescein is ~4 ns) and consequently high emitted photon fluxes that can be achieved even with modest excitation light sources. This property, combined with the variety of different fluorescence modes that can be exploited to advantage in homogeneous assay formats, makes fluorescence detection highly amenable to many high-throughput screening applications (see page 47, right column).

The person of ordinary skill in the art would have had a reasonable expectation of success in substituting biotinylated NAD+ with fluorescence-labeld NAD+ because fluorescence labeling has been well known and practiced in the art.

M.P.E.P. §2144.06 states "In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior

art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963)."

Therefore, the substitution of biotinylation from Trevigen Instruction of the fluorescently labeled NAD+ of Armstrong et al. in an assay of ADP-ribosylating enzyme would have been obvious because Sundberg discloses colorimetric, fluorescent or luminescent read-out as an alternative method for a detection/quantification system (p. 49, right column). Therefore, these may be considered to be art-accepted equivalents.

In addition, various different fluorescence labels such as Texas red, rhodamine, or CyDye are well known equivalents for fluorescent labeling of chemicals as supported by Human Molecular Genetics (supra).

One of skill in the art would have been motivated at the time of invention to make this substitution in order to quantify the PARP activity as suggested by Trevigen with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references.

Furthermore, it would have been obvious to a person of ordinary skill in the art to try different labels available in the art as a detection means, and there are a known number of alternatives/equivalent dyes or labels suitable for the purpose of labeling a

molecule.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

## ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 9:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taeyoon Kim, Ph.D.
Assistant Examiner
AU-1651

Leon B. Lankford, Jr.
Primary Examiner
AU-1651